

CLAIMS

1. A method of modulating NF- κ B dependent gene expression in a cell said method comprised of modulating IKK α activity in the cell.

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2. The method of claim 1 wherein the expression of said NF- κ B dependent gene is inhibited.

3. The method of claim 1 wherein IKK α activity is modulated by administration to a cell of siRNA directed to IKK α .

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4. The method of claim 3 wherein the transcription of said gene is modulated by administration of an siRNA selected from the list consisting of the compositions of SEQ. ID. NO. 2, SEQ. ID. NO. 3, SEQ. ID. NO. 4, SEQ. ID. NO. 5, SEQ. ID. NO 6 or SEQ. ID NO. 7.

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5. A method for selectively modulating expression of a gene whose expression is regulated by IKK α , the method comprising modulating IKK α activity such that expression of said gene is modulated.

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6. The method of claim 5, wherein the transcription of said gene is modulated by administration of an siRNA selected from the list consisting of the compositions of SEQ. ID NO. 2, SEQ. ID NO. 3, SEQ. ID NO. 4, SEQ. ID NO. 5, SEQ. ID NO. 6, or SEQ. ID NO. 7.

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7. The method of claim 5 wherein said gene is selected from the list consisting of IL-6, IL-8, Cox-2, ISG-15, IL-11, or GRO1.

8. The method of claim 5, wherein IKK α activity is modulated by administration of siRNA directed to IKK α .

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9. An siRNA composition comprised of siRNA sequence selected from the list consisting of SEQ. ID NO. 2, SEQ. ID NO. 3, SEQ. ID NO. 4, SEQ. ID NO. 5, SEQ. ID NO. 6, or SEQ. ID NO. 7.
- 5 10. An siRNA composition of claim 9 comprised of siRNA sequence of SEQ. ID NO. 2.
11. An siRNA composition of claim 9 comprised of siRNA sequence of SEQ. ID NO. 3.
- 10 12. An siRNA composition of claim 9 comprised of siRNA sequence of SEQ. ID NO. 4.
13. An siRNA composition of claim 9 comprised of siRNA sequence of SEQ. ID NO. 5.
- 15 14. An siRNA composition of claim 9 comprised of siRNA sequence of SEQ. ID NO. 6.
- 20 15. An siRNA composition of claim 9 comprised of siRNA sequence of SEQ. ID NO. 7.
16. A method for treating autoimmune and inflammatory disease in a mammal said method comprised of modulating the expression or activity of IKK α .
- 25 17. The method of claim 16 wherein the autoimmune and inflammatory disease is selected from the list consisting of asthma, SLE, rheumatoid arthritis, inflammatory bowel disease, and psoriasis.
- 30 18. The method of claim 16 wherein said disease is asthma.

19. The method of claim 16 wherein said disease is SLE.

20. The method of claim 16 wherein the IKK α activity is reduced by administering to a cell siRNA directed to IKK α .

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21. A method for identifying a compound for the treatment of autoimmune and inflammatory disease, said method comprised of the steps of:

a) incubating an IKK α protein in the presence of a potential inhibitor of IKK α activity;

10 b) measuring the loss of IKK α activity;

c) comparing the amount of IKK α activity present in the absence of a potential inhibitor.

22. The method of Claim 21 using a protein fragment of the IKK α protein.

15 23. The method of Claim 21 wherein the IKK α protein is substantially purified.

24. An siRNA compound 21-25 nucleotides in length that specifically hybridizes to a nucleic acid molecule encoding human IKK α of SEQ. ID. No. 1.

SEQ. ID NO. 1

ATGGAGCGGCCCCCGGGGCTGCGGCCGGGCGCGGGCGGGCCCTGGGAGAT
GCGGGAGCGGCTGGGCACCGGCGGCTTCGGGAACGTCTGTCTGTACCAGC
5 ATCGGGAACCTTGATCTCAAAATAGCAATTAAGTCTTGTGCGCTAGAGCTA
AGTACCAAAAACAGAGAACGATGGTGCCATGAAATCCAGATTATGAAGAA
GTTGAACCATGCCAATGTTGTAAAGGCCTGTGATGTTCCCTGAAGAATTGA
ATATTTTGATTTCATGATGTGCCTCTTCTAGCAATGGAATACTGTTCTGGA
GGAGATCTCCGAAAGCTGCTCAACAAACCAGAAAATTGTTGTGGACTTAA
10 AGAAAGCCAGATACTTTCTTTACTAAGTGATATAGGGTCTGGGATTTCGAT
ATTTGCATGAAAACAAAATTATACATCGAGATCTAAAACCTGAAAACATA
GTTCTTCAGGATGTTGGTGGAAGATAATACATAAAATAATTGATCTGGG
ATATGCCAAAGATGTTGATCAAGGAAGTCTGTGTACATCTTTTGTGGGAA
CACTGCAGTATCTGGCCCCAGAGCTCTTTGAGAATAAGCCTTACACAGCC
15 ACTGTTGATTATTGGAGCTTTGGGACCATGGTATTTGAATGTATTGCTGG
ATATAGGCCTTTTTTGCATCATCTGCAGCCATTTACCTGGCATGAGAAGA
TTAAGAAGAAGGATCCAAAGTGTATATTTGCATGTGAAGAGATGTCAGGA
GAAGTTCGGTTTTAGTAGCCATTTACCTCAACCAAATAGCCTTTGTAGTTT
AATAGTAGAACCCATGGAAAACCTGGCTACAGTTGATGTTGAATTGGGACC
20 CTCAGCAGAGAGGAGGACCTGTTGACCTTACTTTGAAGCAGCCAAGATGT
TTTGTATTAATGGATCACATTTTGAATTTGAAGATAGTACACATCCTAAA
TATGACTTCTGCAAAGATAATTTCTTTCTGTTACCACCTGATGAAAGTC
TTCATTCACTACAGTCTCGTATTGAGCGTGAAACTGGAATAAATACTGGT
TCTCAAGAACTTCTTTCAGAGACAGGAATTTCTCTGGATCCTCGGAAACC
25 AGCCTCTCAATGTGTTCTAGATGGAGTTAGAGGCTGTGATAGCTATATGG
TTTATTTGTTTGATAAAAGTAAACTGTATATGAAGGGCCATTTGCTTCC
AGAAGTTTATCTGATTGTGTAAATTATATTGTACAGGACAGCAAAATACA
GCTTCCAATTATACAGCTGCGTAAAGTGTGGGCTGAAGCAGTGCATATG
TGTCTGGACTAAAAGAAGACTATAGCAGGCTCTTTCAGGGACAAAGGGCA
30 GCAATGTTAAGTCTTCTTAGATATAATGCTAACTTAACAAAAATGAAGAA
CACTTTGATCTCAGCATCACAACTGAAAGCTAAATTGGAGTTTTTTC
ACAAAAGCATTTCAGCTTGACTTGGAGAGATACAGCGAGCAGATGACGTAT
GGGATATCTTCAGAAAAAATGCTAAAAGCATGGAAAGAAATGGAAGAAAA
GGCCATCCACTATGCTGAGGTTGGTGTCAATTGGATACTGGAGGATCAGA
35 TTATGTCTTTGCATGCTGAAATCATGGAGCTACAGAAGAGCCCCCTATGGA
AGACGTCAGGGAGACTTGATGGAATCTCTGGAACAGCGTGCCATTGATCT
ATATAAGCAGTTAAAACACAGACCTTCAGATCACTCCTACAGTGACAGCA
CAGAGATGGTGAAATCATTGTGCACACTGTGCAGAGTCAGGACCGTGTG
CTCAAGGAGCTGTTTGGTCATTTGAGCAAGTTGTTGGGCTGTAAGCAGAA
40 GATTATTGATCTACTCCCTAAGGTGGAAGTGGCCCTCAGTAATATCAAAG
AAGCTGACAATACTGTCATGTTTCATGCAGGGAAAAAGGCAGAAAGAAATA
TGGCATCTCCTTAAAATTGCCTGTACACAGAGTTCTGCCCCGTCCCTTGT
AGGATCCAGTCTAGAAGGTGCAGTAACCCCTCAGACATCAGCATGGCTGC
CCCCGACTTCAGCAGAACATGATCATTCTCTGTCATGTGTGGTAACTCCT
45 CAAGATGGGGAGACTTCAGCACAAATGATAGAAGAAAATTTGAACTGCCT
TGGCCATTTAAGCACTATTATTCATGAGGCAAATGAGGAACAGGGCAATA
GTATGATGAATCTTGATTGGAGTTGGTTAACAGAATGA

SEQ ID NO. 2

IKK α _3 Targeted Region (mRNA) AAGCAGUGCACUAUGUGUCUG
Sense siRNA: 5'-GCAGUGCACUAUGUGUCUG*dTdT*-3'
Antisense siRNA:5'-CAGACACAUAGUGCACUGC*dTdT*-3'

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SEQ ID NO. 3

IKK α _3 Inverted
Sense siRNA: 5'-GUCUGUGUAUCACGUGACG*dTdT*-3'
Antisense siRNA:5'-CGUCACGUGAUACACAG*dTdT*-3'

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SEQ ID NO. 4

IKK α _1 Targeted Region (mRNA) AACACUGCAGUAUCUGGCCCC
Sense siRNA: 5'-CACUGCAGUAUCUGGCCCC*dTdT*-3'
Antisense siRNA:5'-GGGGCCAGAUACUGCAGUG*dTdT*-3'

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SEQ ID NO. 5

IKK α _2 Targeted Region (mRNA) AAUUGGGACCCUCAGCAGAGA
Sense siRNA: 5'-UUGGGACCCUCAGCAGAG*dTdT*-3'
Antisense siRNA:5'-UCUCUGCUGAGGGUCCCA*dTdT*-3'

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SEQ ID NO. 6

IKK α _4 Targeted Region (mRNA) AAGGCCAUCCACUAUGCUGAG
Sense siRNA: 5'-GGCCAUCCACUAUGCUGAG*dTdT*-3'
Antisense siRNA:5'-CUCAGCAUAGUGGAUGGCC*dTdT*-3'

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SEQ ID NO. 7

IKK α _4 Inverted
Sense siRNA: 5'- GAGUCGUAUCACCUACCGG*dTdT*-3'
Antisense siRNA:5'- CCGGUAGGUGAUACGACUC*dTdT*-3'

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SEQ ID NO.8

MERPPGLRPGAGGPWEMRERLGTGGFGNVCLYQHRELDLKIAIKSCRLEL
STKNRERWCHEIQIMKKLNHANVVKACDVPEELNILIHDVPLLAMEYCSG
GDLRKLLNKPENCCGLKESQILSLLSDIGSGIRYLHENKIIHRDLKPENI
35 VLQDVGGKIIHKIIDLGYAKDVDQGSLSCTSFVGTLOYLAPELFENKPYTA
TVDYWSFGTMVFECIAGYRPFLLHHLQPFTHWEKIKKKDPKCIFACEEMSG
EVRFSSHLPPQNSLCSLIVEPMENWLQMLNWDPPQRRGGPVDLTLKQPRC
FVLMDHILNLKIVHILNMTSAKIIISFLLPPDESLHSLQSRIERETGINTG
SQELLSETGISLDPKRPASQCVLDGVRGCDSYMVYLFDKSKTVYEGPFAS
40 RSLSDCVNYIVQDSKIQLPITQLRKVWAEAVHYVSGLKEDYSRLFQGGQRA
AMLSLLRYNANLTKMKNTLISASQQLKAKLEFFHKSIIQLDLERYSEQMTY
GISSEKMLKAWKEMEKAIIHYAEVGVIGYLEDQIMSLHAEIMELQKSPYG
RRQGDLMESLEQRAIDLKQLKHRPSDHSYSDDSTEMVKIIVHTVQSQDRV
LKELFGHLSKLLGCKQKIIDLLPKVEVALSNIKEADNTVMFMQGRQKEI
45 WHLLKIIACTQSSARSLVGSSLEGAVTPQTSAWLPPTSAEHDHSLSCVVTP
QDGETSAQMIEENLNCLGHLSTIIHEANEEQGNMMLNDWSWLTE

Case 9/263 US

SEQ. ID. No. 9

Forward primer 5'-GCACAGAGATGGTGAAAATCATTG-3'

5 SEQ. ID. No. 10

Reverse primer 5'-CAACTTGCTCAAATGACCAAACAG-3'.

SEQ. ID. No. 11

The probe sequence 5'-TGAGCACACGGTCCTGACTCTGCA